

Does allergen immunotherapy impact the susceptibility and severity of COVID-19?

Ya-dong Gao¹, Wang Yin², Huan Chen³, Xiang Dong¹, Hao Chen², Hui-ling Liang¹, Yaqi Yang², Yan-dan Chen³, and Rongfei Zhu²

¹Zhongnan Hospital of Wuhan University

²Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology

³Affiliated Hospital of Hubei Polytechnic University

February 11, 2023

Does allergen immunotherapy impact the susceptibility and severity of COVID-19?

To the editor,

Allergic asthma (AA) and allergic rhinitis (AR) might be protective against SRAS-CoV-2 infection and progress to severe disease of coronavirus disease 2019 (COVID-19)¹. COVID-19 vaccination was safe and well tolerated in patients receiving allergen immunotherapy (AIT)^{2,3}, and the adherence to subcutaneous immunotherapy (SCIT) was not affected during COVID-19 pandemic⁴. Whether AIT impacts the susceptibility and severity of COVID-19 is still unknown. In December 2022, China ended its “Zero-COVID” policy and more than 70% of the population got infected with SARS-CoV-2 within one month. We conducted an online WeChat questionnaire between 3rd Jan and 10th Jan 2023 to investigate the infection and hospitalization rates and symptom duration of COVID-19 in AR and/or AA patients receiving SCIT with house-dust mite (HDM) extract in China. The relatives of these SCIT patients, who did not receive SCIT, were also surveyed and divided into two groups: allergy group and non-allergy group. The study was approved by the Medical Ethic Committee of Tongji Hospital of Huazhong University of Science and Technology (Approval Number: TJ-IRB20230204). The informed consent was waived since the voluntary nature of responding to the questionnaire.

A total of 1246 SCIT patients and 1078 of their relatives (370 allergic and 708 non-allergic) responded to the questionnaire. SCIT patients were generally younger than allergy and non-allergy group. The proportion of male were higher in SCIT patients compared to allergy and nonallergy group. 82.4% of the SCIT patients were diagnosed with AR, only 5.3% were asthmatics, and the rest were AR with asthma (12.3%). The average duration of AIT was 1.4 ± 1.3 years. SCIT patients had a lower proportion of both at least one dose and completed three doses of COVID-19 vaccines when compared to allergy and non-allergy group ($P = 0.000$) (Table S1).

Most respondents had been infected with SARS-CoV-2. SCIT was associated with a lower infection rate (78.6%) compared to allergy (81.4%) and non-allergy group (81.5%) ($P < 0.0001$) (Table S2). The duration of COVID-19 symptoms was shorter in SCIT group (5.7 ± 4.0 days) compared to allergy group (7.0 ± 4.5 days, $P = 0.000$) and non-allergy group (7.7 ± 4.4 days, $P = 0.000$) (Table S2). The hospitalization rate was 0.4% in SCIT group, which was significantly lower than that in non-allergy group (1.73%) ($P = 0.008$).

We then performed a two-to-one matching of SCIT group with allergy and non-allergy group to adjust age and sex difference between the three groups. The infection rate was still slightly lower in SCIT group compared

to allergy and non-allergy group (78.3% vs. 81.9%, 81.4%). The duration of symptoms and hospitalization rate did not show much difference among three groups after adjusting (Table 1).

Moreover, we found that patients receiving 6-12 months SCIT had a shorter duration of symptoms caused by SARS-CoV-2 infection compared to those in SCIT course < 6 months and those receiving SCIT > 12 months, even though only one fourth of them completed three doses of COVID-19 vaccines (Table 2). shorter duration of symptoms. The duration of SCIT has no impacts on both infection and hospitalization rate (Table 2).

A lower expression of angiotensin converting enzyme 2 (ACE2) in airway epithelia⁵ may contribute to the protecting effect of type 2 inflammation against SARS-CoV-2 infection and severe COVID-19⁶. This study revealed an almost same infection rates in allergic and non-allergic individuals after adjusting age and sex, suggesting ACE2 expression level had no effect on Omicron infection. More importantly, SCIT patients has a slightly lower infection rate compared to allergy and non-allergy groups, suggesting that repeated allergen stimulation during SCIT in HDM-sensitized individuals may elicit a strong T cell response with ability to cross-react with SARS-CoV-2, as demonstrated in silico analysis⁷, which may protect SCIT individuals from infection. The proportion with three doses COVID-19 vaccines were significantly lower in SCIT patients, albeit SCIT was reported to dampen immune responses to SARS-CoV-2 vaccines⁸, the infection rate of SARS-CoV-2 was still lower in SCIT patients. We also observed a shorter duration of symptoms due to SARS-CoV-2 infection in those receiving 6-12 months HDM-SCIT compared to those receiving < 6 months and > 12 months HDM-SCIT, consistent with previous studies showing the immune responses to SCIT reach a peak during 6-12 months⁹. EAACI stated recently in a position paper that AIT and COVID-19 immune responses do not seem to interfere negatively, and AIT patients might even benefit from AIT¹⁰. Thus, our results for the first time demonstrated that SCIT may have a protective effect against SARS-CoV-2 infection, especially immediately after completing the dose-escalation phase.

KEYWORDS: Allergic rhinitis; Allergen immunotherapy; SARS-CoV-2; Coronavirus disease 2019; Infection

CONFLICT OF INTEREST: The authors declare that they have no conflicts of interest.

Author Contributions: YDG, RFZ and YDC conceived the study, YW and HuC designed the questionnaire and collected data. XD, HaC, YQY and HLL dispensed the questionnaire and monitored the survey. RFZ analyzed the data and YDG wrote the manuscript. All authors contributed to the final review.

Acknowledgment : We thank all members of Hubei Provincial Doctors Association Allergic Physicians Branch for their help in the recruitment of patients and relatives into this study.

Funding information: none.

Yin Wang¹

Huan Chen²

Xiang Dong³

Hao Chen¹

Hui-ling Liang³

Ya-qi Yang¹

Yan-dan Chen²

Rong-fei Zhu¹

Ya-dong Gao³

1. Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

2. Department of Otolaryngology-Head and Neck Surgery and Allergy, Central Hospital of Huangshi City, Huangshi, China
3. Department of Allergology, Zhongnan Hospital of Wuhan University, Wuhan China

Correspondence:

Ya-dong Gao, Department of Allergology, Zhongnan Hospital of Wuhan University, Donghu Road 169, Wuhan 430071, China

Email: gaoyadong@whu.edu.cn

Rong-fei Zhu, Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1095 Jiefang Avenue, Wuhan 430030, China

Email: zrf13092@163.com

Yan-dan Chen, Department of Otolaryngology-Head and Neck Surgery and Allergy, Central Hospital of Huangshi City, Tianjin Road 141, Huangshi 435002, China

Email: 47823296@qq.com

Yin Wang and Huan Chen contributed equally.

REFENRECES

1. Zhang HP, Sun YL, Wang YF, et al. Recent developments in the immunopathology of COVID-19. *Allergy*. 2022.
2. Xu Y, Guan K. Real-life data on inactivated COVID-19 vaccination in patients with subcutaneous allergen immunotherapy. *Clin Transl Allergy*. 2022;12(1):e12115.
3. Pfaar O, Agache I, Bonini M, et al. COVID-19 pandemic and allergen immunotherapy-an EAACI survey. *Allergy*. 2021;76(11):3504-3516.
4. Yegit OO, Demir S, Unal D, et al. Adherence to subcutaneous immunotherapy with aeroallergens in real-life practice during the COVID-19 pandemic. *Allergy*. 2022;77(1):197-206.
5. Wang H, Song J, Yao Y, et al. Angiotensin-converting enzyme II expression and its implication in the association between COVID-19 and allergic rhinitis. *Allergy*. 2021;76(3):906-910.
6. Bloom CI, Cullinan P, Wedzicha JA. Asthma Phenotypes and COVID-19 Risk: A Population-based Observational Study. *Am J Respir Crit Care Med*. 2022;205(1):36-45.
7. Balz K, Kaushik A, Chen M, et al. Homologies between SARS-CoV-2 and allergen proteins may direct T cell-mediated heterologous immune responses. *Sci Rep*. 2021;11(1):4792.
8. Yao Y, Huang A, Deng YK, et al. Allergen Immunotherapy Reverses Immune Response to SARS-CoV-2 Vaccine in Patients with Allergic Rhinitis: A Prospective Observational Trial. *Am J Respir Crit Care Med*. 2022;206(6):780-783.
9. Durham SR, Shamji MH. Allergen immunotherapy: past, present and future. *Nat Rev Immunol*. 2022;1-12.
10. Jutel M, Torres MJ, Palomares O, et al. COVID-19 vaccination in patients receiving allergen immunotherapy (AIT) or biologicals-EAACI recommendations. *Allergy*. 2022;77(8):2313-2336.

Hosted file

Table1,table 2.doc available at <https://authorea.com/users/320601/articles/623908-does-allergen-immunotherapy-impact-the-susceptibility-and-severity-of-covid-19>